APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,359	07/30/2001	D. Wade Walke	LEX-0208-USA	1068

24231   7590   12/13/2002

LEXICON GENETICS INCORPORATED
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THE WOODLANDS, TX 77381-1160

EXAMINER
MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

		Application No.	**Applicant(s)**
		09/918,359	WALKE ET AL.
Office Action Summary		**Examiner**	**Art Unit**
		Joseph F Murphy	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed
  after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any
  earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on <u>03 October 2002</u> .

2a) ☐ This action is **FINAL.**   2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is
closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1 and 5-9* is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1 and 5-9* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
    If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a) ☐ All b) ☐ Some * c) ☐ None of:

      1. ☐ Certified copies of the priority documents have been received.

      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .

      3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage
        application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

    a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>5</u> .

4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison A* .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group III in Paper No. 7, 10/32002 is

acknowledged.

Specification

The title of the invention is not descriptive. Applicant should avoid the use of novel in

the title, as patents are presumed to be novel and unobvious.

Claim Rejections - 35 USC §§ 101, 112, first paragraph

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new
and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and
using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or
with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the
inventor of carrying out his invention.

Claims 1, 5-9 are rejected under 35 U.S.C. § 101 because they are drawn to an invention

with no apparent or disclosed patentable utility. The instant application has provided a

description of an isolated DNA encoding a protein and the protein encoded thereby. The instant

application does not disclose the biological role of this protein or its significance. Applicant is

directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-

1099, Friday January 5, 2001.

It is clear from the instant specification that the nucleic acid encoding the NHP

polypeptide has been isolated because of its similarity to known proteins. However, it is

commonly known in the art that sequence-to-function methods of assigning protein function are

prone to errors (Doerks et al.1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al. page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). Furthermore, Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

After complete characterization, this protein may be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson,* 148 USPQ 689 (Sup. Ct., 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation.

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However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 USC § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a nucleic acid encoding a polypeptide which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as NHP, the instant invention is incomplete. In the absence of knowledge of the natural substrate or biological significance of this protein, there is no immediately obvious <u>patentable</u> use for it. To employ a protein of the instant invention in the identification of substances which inhibit its activity is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for NHP then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

Claims 1, 5-9 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if, arguendo, the nucleic acid encoding the NHP protein is found to have a patentable utility, claim 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding an amino acid of SEQ ID NO: 7, or a nucleic acid with the sequence as set forth in SEQ ID NO: 6, does not reasonably provide enablement for a nucleic acid which hybridizes to SEQ ID NO: 6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 5 are overly broad since insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which will retain the characteristics of NHP. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of NHP. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

Since the claims encompass variant nucleic acids and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8

USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors considered to be relevant in the instant case are set forth below:

(1) the breadth of the claims - The claims are drawn to a nucleic acid which hybridizes to SEQ ID NO: 6.

(2) the nature of the invention - The instant invention is a nucleic acid which hybridizes to SEQ ID NO: 6.

(3) the state of the prior art - The Voet reference demonstrates that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function.

(5) the level of predictability in the art - The Voet reference demonstrates the unpredictability of the protein art.

(6) the amount of direction provided by the inventor - Applicant has only taught a nucleic acid with a sequence as set forth in SEQ ID NO: 7, and the polypeptide of SEQ ID NO: 7.

(7) the existence of working examples - Working examples are not provided for NHP.

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 5 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to a nucleic acid which hybridizes to SEQ ID NO: 6. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the encoded SEQ ID NO: 7. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a nucleic acid with a sequence as set forth in SEQ ID NO: 6, and the polypeptide of SEQ ID NO: 7 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative

number of species to describe the genus. Thus, applicant was not in possession of the claimed

genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing

to particularly point out and distinctly claim the subject matter which applicant regards as the

invention.

Claim 5 recites the term "highly stringent conditions", which is a conditional term and

renders the claim indefinite. The metes and bounds of the claim thus cannot be ascertained.

This rejection could be obviated by supplying specific conditions supported by the specification

which Applicant considers to be "highly stringent".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the

basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al. (1997).

The EST AA309878 is a nucleic acid which is 28.5% identical to SEQ ID NO: 6, and

would hybridize to SEQ ID NO: 6 under "highly stringent conditions, see Sequence Comparison

A, attached. Thus claim 5 is anticipated.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
December 10, 2002

LOCUS   AA309878

DEFINITION EST180740 Jurkat T-cells V Homo sapiens cDNA 5' end, mRNA sequence.

ACCESSION AA309878

VERSION   AA309878.1 GI:1962217

KEYWORDS   EST.

SOURCE   human.

ORGANISM   Homo sapiens
           Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
           Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 431)

AUTHORS   Adams,M.D., Kerlavage,A.R., Fleischmann,R.D., Fuldner,R.A., Bult
           ,C.J., Lee,N.H., Kirkness,E.F., Weinstock,K.G., Gocayne,J.D., White
           ,O., Sutton,G., Blake,J.A., Brandon,R.C., Man-Wai,C., Clayton,R.A.,
           Cline,T.R., Cotton,M.D., Earle-Hughes,J., Fine,L.D., Fitzgerald
           ,L.M., Fitzhugh,W.M., Fritchman,J.L., Geoghagen,N.S., Glodek,A.,
           Gnehm,C.L., Hanna,M.C., Hedblom,E., Hinkle,P.S.Jr., Kelley,J.M.,
           Kelley,J.C., Liu,L.I., Marmaros,S.M., Merrick,J.M.,
           Moreno-Palanques,R.F., McDonald,L.A., Nguyen,D.T., Pellegrino,S.M.,
           Phillips,C.A., Ryder,S.E., Scott,J.L., Saudek,D.M., Shirley,R.,
           Small,K.V., Spriggs,T.A., Utterback,T.R., Weidman,J.F., Li,Y.,
           Bednarik,D.P., Cao,L., Cepeda,M.A., Coleman,T.A., Collins,E.J., He,W.W.
           Dinke,D., Feng,D.-F., Ferrie,A., Fischer,C., Hastings,G.A., He,W.W.,
           , Hu,J.S., Greene,J.M., Gruber,J., Hudson,J., Kim,A.K., Kozak,D.L.,
           Kunsch,C., Hungjun,J., Li,H., Meissner,P.S., Olsen,H., Raymond,L.,
           Wei,Y.F., Wing,J., Xu,C., Yu,G.L., Ruben,S.M., Dillon,P.J., Fannon
           ,M.R., Rosen,C.A., Haseltine,W.A., Fields,C., Fraser,C.M. and
           Venter,J.C.

TITLE   Initial assessment of human gene diversity and expression patterns
           based upon 83 million nucleotides of cDNA sequence

JOURNAL   Nature 377 (6547 Suppl), 3-174 (1995)

MEDLINE   96026280

COMMENT   Contact: Kerlavage, AR
           Bioinformatics
           The Institute for Genomic Research
           9712 Medical Center Drive, Rockville, MD 20850 USA
           Tel: 3018699056
           Fax: 3018699423
           Email: arkerlav@tigr.org
           For clone availability, additional sequence and expression
           information related to this EST, please check the TIGR Human Gene
           Index (http://www.tigr.org/tdb/hgi/hgi.html)
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ORIGIN

Several comparison

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Best Local Similarity   98.8%; Pred. No. 4.1e-81;
Matches 416; Conservative 0; Mismatches 5; Indels 0; Gaps 0;

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RESULT 4

BF537032

LOCUS   BF537032   994 bp   mRNA   linear   EST 11-DEC-2000

DEFINITION 6020048936F1 NCI_CGAP_SG2 Mus musculus cDNA clone IMAGE:4188321 5',
           mRNA sequence.

ACCESSION BF537032

VERSION   BF537032.1 GI:11624400

KEYWORDS   EST.

SOURCE   mouse.

ORGANISM   Mus musculus
           house mouse.
           Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
           Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.

REFERENCE 1 (bases 1 to 994)

AUTHORS   NIH-MGC http://mgc.nci.nih.gov/.

TITLE   National Institutes of Health, Mammalian Gene Collection (MGC)

JOURNAL   Unpublished (1999)

COMMENT   Contact: Robert Strausberg, Ph.D.
           Email: cgapbs-r@mail.nih.gov
           Tissue Procurement: Jeffrey E. Green, M.D.
           cDNA Library Preparation: Life Technologies, Inc.
           cDNA Library Arrayed by: The I.M.A.G.E. Consortium (LLNL)
           DNA Sequencing by: Incyte Genomics, Inc.
           Clone distribution: MGC clone distribution information can be
           found through the I.M.A.G.E. Consortium/LLNL at:
           http://image.llnl.gov
           Plate: LLAM9512 row: g column: 10
           High quality sequence stop: 728.

FEATURES   Location/Qualifiers
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                     Technologies. Note: this is a NCI_CGAP Library."

BASE COUNT   247 a   242 c   284 g   221 t

ORIGIN

Query Match   26.7%; Score 390; DB 10; Length 994;
Best Local Similarity   76.5%; Pred. No. 2.2e-75;
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Qy   775 CCGTTGTCCTGCTGTGGAGGCCGGGAGATGGTGGGCGCCCTGGTTGTGGGACAGACCCGC 834
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Db   8 CCGGCACTCAGGATGGAAGCCAGAGACAGTATGGCCCCACTGTCGCCTTCGGGGACATGACACGA 67

Qy   835 ATGCTGAACAATGCTCATGCTGTGTTCCGGCGTATCATCCCCAGCATGAAGCCGATG 894
          || ||||||| || | ||||||| |||||||| ||||||||||||||| ||| ||||||
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